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# LETTERS AND CORRESPONDENCE

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## Acute Intravascular Haemolytic Transfusion Reaction Due to Anti-c Undetected by Conventional Pretransfusion Cross-Matching Tests

*To the Editor:* Although red cell alloantibodies causing immune mediated intravascular hemolysis are usually detectable by conventional pretransfusion serological testing, occasionally a severe haemolytic transfusion reaction (HTR) can occur in patients receiving blood transfusions that are compatible according to conventional techniques such as saline indirect antiglobulin test (S-IAT) or enzyme IAT (E-IAT). In these cases, more sensitive techniques such as the manual polybrene test IAT [1] or poly ethylene glycol (PEG)-IAT [2] may be required for their detection. We describe herein a patient who experienced severe intravascular HTR following the transfusion of red cells compatible according to the conventional cross-matching testing.

A 52-year-old female, S.D., who had chronic liver disease with severe gastrointestinal bleed was admitted to the Gastroenterology Department at our medical institution. She had had three uneventful pregnancies, the last of which had occurred 17 years earlier. She underwent a hysterectomy 10 years ago during which she was transfused with two units of blood without any complications. Presently, she received two units (units 1 and 2) of group O Rh positive packed red cells compatible by S-IAT and E-IAT. Her pretransfusion Hb level was 6.7 gm/dl. The transfusion of the first unit was uneventful. However, the patient developed fever (105°F) and chills with dyspnoea and bilateral loin pain following transfusion of about 10 ml of blood from the second unit. Transfusion was stopped immediately and blood and urine samples were collected for routine investigation of transfusion reaction. A posttransfusion urine sample was red coloured and strongly positive for haemoglobin (Hb). Laboratory investigations confirmed that the patient had an attack of severe intravascular hemolysis as evidenced by the fall of the Hb level to 4.8 gm/dl, elevated serum bilirubin level (270 mmol/L), and decreased serum haptoglobin level (84 mg/dl). A major mismatch was ruled out by repeating ABO grouping, Rh typing, and compatibility testing using conventional techniques. A potent anti-c was demonstrated in the pre- and post-transfusion serum samples of the patient using PEG-IAT with the titre of 128. Both S-IAT and E-IAT failed to detect the offending antibody in pre- as well as post-transfusion samples. Presence of anti-c was further confirmed by testing the patient's serum with three c negative and three c positive blood samples with PEG-IAT. All c positive red cells showed strong positive reaction against the patient's serum. Detailed Rh genotyping was performed on the pretransfusion sample of the patient's and on the transfused donor units. The first blood unit was found to be negative for the presence of c antigen, but positive results were obtained for the second unit. (Table I). Treatment of the patients serum with dithiothreitol (DTT) resulted in a weak reaction indicating that the anti-c was of both immunoglobulin (Ig)G and IgM classes. Subsequently, the patient was managed conservatively with transfusion of c negative blood without any further complication

**TABLE I. Results of Rh Genotyping***

| | Rh genotyping | | | | | |
|---|---|---|---|---|---|---|
| Sample | C | D | E | c | e | HTR |
| Patient | + | + | − | − | + | |
| Unit 1 | + | + | + | − | − | No HTR |
| Unit 2 | + | + | − | + | − | Severe HTR |

*HTR, haemolytic transfusion reaction.

Severe intravascular HTR has been reported in a patient who received blood compatible in vitro with conventional cross-match techniques. Both S-IAT and E-IAT failed to detect the offending Rh antibody (anti-c) in either pre- or post-transfusion samples of the patient. However, PEG-IAT was most sensitive in the detection of antibody. This rare case of severe acute HTR by antibody other than ABO illustrates the fact that properly performed testing for serological compatibility before blood transfusion will not always detect clinically significant antibody. Others have also reported HTR attributable to antigens in the Rh system not detectable by conventional serological techniques [3,4]. Although most Rh antibodies do not fix complement [5] and cause red cell destruction extravascularly, rare examples of Rh antibodies implicated in intravascular hemolysis have been reported [3]. The present report serves as an example that Rh antibodies do occasionally fix complement and cause intravascular hemolysis.

**DILESHWARI PRADHAN**
*Senior resident, Department of Transfusion Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India*
**RAJENDRA CHAUDHARY**
*Associate Professor, Department of Transfusion Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India*

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## Trisomy 10 in Adult Pre–B-Cell Leukemia

*To the Editors:* According to the recent literature published by Morgan et al. [1], trisomy 10 as the sole abnormality appears to be associated exclusively with acute lymphoblastic leukemia (ALL) in children and with Acute Myeloblastic Leukemia (AML) in adult. And in the review by Faderl et al. [2] that focuses on the most important chromosomal abnormalities found in adult ALL, it was not reported. However, we experienced a case of ALL with the same chromosome abnormality in adult.

A 40-year-old female was admitted to our hospital for fever and headache. Physical examination revealed anemia with no hepatosplenomegaly or lymphadenopathy. Her complete blood count showed a hemoglobin of 7.1 g/dl, white blood cells of 2,900/μl, including 10% blasts, and platelets of $27.1 \times 10^4/\mu l$. Coagulation screen was normal. Biochemical results were all within normal limits. Bone marrow aspiration showed infiltration with 88.2% blasts, which were negative for peroxydase stain and weakly positive for periodic-acid Schiff one. Immunophenotyping of the blasts was positive for CD10, CD19, and HLA-DR. Thus she was diagnosed as pre–B-cell ALL (FAB-L1). Cytogenetic analysis was performed using a standard cytogenetic method. Of 30 metaphases studies, three revealed trisomy 10: 47,XX as the sole abnormality at the time of diagnosis, and the remaining cells appeared of normal karyotype. She received induction chemotherapy with adriamycin, vincristine, cyclophosphamide, L-asparaginase, and oral predonisone. After the treatment she achieved complete remission (CR) with disappearance of the chromosome abnormality and remains in CR for two years to date.

It is important to investigate certain cytogenetic features of leukemic cells for directing therapy and predicting outcome. As reviewed by Harris et al. [3], of all hyperdiploid ALL among children, a subgroup with both trisomy 4 and 10 has an extremely favorable prognosis [3]. But as a sole abnormality, trisomy 10 is rare; only 12 cases have been described in the literature—seven were patients with ANLL, all of whom were adults, and five with ALL, all of whom were children [1,4]. In addition, the pediatric group has more prognostically favorable clinical features than the adult group [1]. Therefore, trisomy 10 seems to be associated with characteristics related to patient age and leukemic lineage, the cause of which is not entirely clear.

Herein we describe the thirteenth case with trisomy 10 as the sole abnormality. This is the first adult ALL patient reported so far [1–3]. Furthermore, our case, despite adult ALL, had a favorable clinical course and remains in CR for 2 years only with conventional chemotherapy. Immunophenotype classified as pre–B-cell ALL, similar to that of the low-risk pediatric group [3,5], might have been associated with this outcome. These results suggest that not only trisomy 10 but also unidentified gene abnormalities that are likely to be detected according to patient age seem to be necessary for such leukemic changes.

**Atsuo Okamura**
**Akinori Yamaguchi**
**Shinichi Shimizu**
**Seizo Kadowaki**
*Department of Internal Medicine, Ono City Hospital, Ono, Japan*
**Kazuo Chihara**
**Toshimitsu Matsui**
*Third Department of Internal Medicine, Kobe University School of Medicine, Kobe, Japan*
**Takao Fujimoto**
**Kaori Kanki**
**Kazuyoshi Fujio**
*Department of Clinical Laboratory, Ono City Hospital, Ono, Japan*

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## Thrombotic Thrombocytopenic Purpura and Hypothyroidism

*To the Editor:* Thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by the classic pentad of microangiopathic hemolytic anemia, thrombocytopenia, neurological abnormalities, fever, and variable renal impairment [1]. We report for the first time, the case of a patient in which reversible hypothyroidism was observed in the course of TTP.

A 42-year-old man was admitted to the hospital in November 1997 because of headache, lethargy, fatigue, and mild right arm weakness. During the preceding 10 days he had had five transient neurologic ischemic attacks. Physical examination revealed purpuric rash on the lower limb. Temperature was 38°C. He was disoriented but was otherwise neurologically normal. Laboratory findings were: thrombocytopenia (platelet count $27 \times 10^9$/L); mechanical hemolytic anemia (hemoglobin 9.7 g/dl, schizocytes 2%, lactate dehydrogenase 842 U/l); serum creatinine 104 μmol/l. Cerebral computed tomography showed no abnormalities. TTP was diagnosed, vincristine was given at a dose of 2 mg and daily plasma exchanges with fresh frozen plasma were begun immediately associated with acetylsalicylic acid (100 mg/d). After five plasma exchanges, remission was achieved and the patient was discharged from the hospital. Initial laboratory results did not demonstrate evidence of an underlying disorder. Thyroid function tests performed because of unusual asthenia at presentation disclosed mild hypothyroidism (TSH 17 μUl/ml, normal range <5 μUl/ml). Thyroid gland was clinically normal. Serum was negative for thyroid autoantibodies. Because the clinical presentation of hypothyroidism was poor, we kept watch without specific therapy. Thyroid function returned to normal value after 6 months. When last seen, in October 1998, the patient remains without symptoms; full blood count and biochemistry are normal.

In TTP, the wide-spread vascular lesion spares practically no organ. The most commonly affected organs seen in postmortem examination include the kidney, brain, heart, spleen, and lung [1]. However, infarction of various endocrine may occur in rare instances. Diabetes mellitus has been reported, presumably the result of islet cell infarction [1]. Diabetes insipi-

dus from neurohypophyseal lesions is also reported [1]. Because thrombotic microangiopathy has been observed previously in the thyroid [2], and because the hypothyroidism was reversible after TTP remission, we postulate that microvascular lesions were involved in the pathogenesis of hypothyroidism; especially autoimmune thyroiditis or hypothyroidism related to antithyroid agents were excluded in our patient.

We conclude that hypothyroidism may complete the commonly agreed upon manifestations of TTP and we recommend screening of thyroid function in TTP.

**J.M. Durand**
**C. Gautier**
**S. Salas**
**F. Retornaz**
**P. Lefevre**
*Department of Internal Medicine, CHU Sainte Marguerite, Marseille, France*

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